

WHAT IS CLAIMED IS:

1. A method for the *in vitro* proliferation of a multipotent neural stem cell comprising the steps of:
  - (a) obtaining neural tissue from a mammal, said neural tissue  
5 containing at least one multipotent neural stem cell capable of producing progeny that are capable of differentiating into neurons and glia;
  - (b) dissociating said neural tissue to obtain a cell suspension comprising said multipotent neural stem cell;
  - 10 (c) culturing said cell suspension in a first culture medium containing at least one proliferation-inducing growth factor to proliferate said neural stem cell and produce neural stem cell progeny; and
  - (d) passaging said neural stem cell progeny to a second culture  
15 medium containing at least one proliferation-inducing growth factor to further proliferate said neural stem cell progeny.
2. The method of claim 1 wherein said proliferation-inducing growth factor is selected from the group consisting of epidermal growth factor, amphiregulin, acidic fibroblast growth factor, basic fibroblast growth factor, transforming growth factor  
20 alpha, and combinations thereof.
3. The method of claim 1 wherein said neural tissue is obtained from a ventricle of said mammal and wherein prior to step (a), a proliferation-inducing growth factor is administered to said ventricle to induce *in vivo* proliferation of said multipotent neural stem cell.
- 25 4. The method of claim 1 further comprising the additional step of:
  - (e) inducing the proliferated neural stem cell progeny to differentiate to produce a cell culture comprising differentiated neural cells.
5. The method of claim 4 wherein said proliferated neural stem cell progeny are

induced to differentiate by culturing said proliferated neural stem cell progeny in a third culture medium containing at least one differentiation-inducing growth factor.

6. The method of claim 4 wherein the proliferated neural stem cell progeny are contacted with a differentiation-inducing substrate.

5 7. A cell culture comprising daughter multipotent neural stem cells that are the progeny of at least one parent multipotent neural stem cell obtained from dissociated mammalian neural tissue and proliferated *in vitro* in a culture medium containing at least one proliferation-inducing growth factor, wherein said daughter multipotent neural stem cells are capable of producing progeny that are capable of  
10 differentiating into neurons, and glia.

8. The cell culture of claim 7 wherein said proliferation-inducing growth factor is selected from the group consisting of epidermal growth factor, amphiregulin, acidic fibroblast growth factor, basic fibroblast growth factor, transforming growth factor alpha, and combinations thereof.

15 9. A method of producing a cell culture comprising non-tumorigenic, genetically modified neural cells comprising the steps of:

- (a) dissociating neural tissue containing at least one multipotent neural stem capable of producing neural stem cell progeny that are capable of differentiating into neurons and glia,
- 20 (b) proliferating said multipotent neural stem cell in a culture medium containing a proliferation-inducing growth factor to produce said neural stem cell progeny, and
- (c) genetically modifying said neural stem cell progeny to produce a cell culture comprising non-tumorigenic, genetically modified neural  
25 stem cell progeny.

10. The method of claim 9 wherein the proliferation-inducing growth factor is selected from the group consisting of acidic fibroblast growth factor, basic fibroblast growth factor, epidermal growth factor, amphiregulin, transforming

growth factor alpha, and combinations thereof.

11. The method of claim 9 wherein said neural stem cell progeny are genetically modified to produce a growth factor product.

12. The method of claim 9 wherein said neural stem cell progeny are genetically modified to produce a neuropeptide.

13. The method of claim 9 further comprising

(d) differentiating said genetically modified neural stem cell progeny to produce a cell culture comprising differentiated neural cells selected from the group consisting of astrocytes, neurons, oligodendrocytes, and combinations thereof.

14. A method of producing non-tumorigenic, genetically modified differentiated neural cells comprising the steps of:

(a) isolating at least one multipotent neural stem cell from donor CNS tissue, said neural stem cell being capable of producing

progeny that are capable of differentiating into neurons and glia,

(b) proliferating the isolated neural stem cells in a culture medium containing a proliferation-inducing growth factor to produce precursor cells,

(c) differentiating the precursor cells, and

(d) genetically modifying said differentiated cells.

15. A cell culture comprising non-tumorigenic, neural stem cell progeny that are capable of differentiating into neurons, and glia.

16. A method of remyelinating a neuron comprising the steps of:

(a) dissociating mammalian neural tissue containing at least one

multipotent stem cell capable of producing neural stem cell progeny that are capable of differentiating into neurons, and glia,

(b) exposing said multipotent stem cell to a culture medium

containing at least one proliferation-inducing growth factor to produce neural stem cell progeny,

(c) harvesting said neural stem cell progeny, and

(d) causing said harvested neural stem cell progeny to come into  
5 contact with a demyelinated axon to effect remyelination of said demyelinated axon.

17. The method of claim 16 wherein said proliferation inducing growth factor is selected from the group consisting of acidic fibroblast growth factor, basic fibroblast growth factor, epidermal growth factor, amphiregulin, transforming  
10 growth factor alpha and combinations thereof. *EGF & TGF $\alpha$*

18. A method of remyelinating a neuron comprising the steps of:  
(a) dissociating mammalian neural tissue containing at least one multipotent stem cell capable of producing neural stem cell progeny that are capable of differentiating into neurons, astrocytes, and  
15 oligodendrocytes,  
(b) exposing said multipotent stem cell to a first culture medium containing at least one proliferation-inducing growth factor to produce neural stem cell progeny,  
(c) differentiating said neural stem cell progeny in a second culture  
20 medium that is substantially free of said proliferation-inducing factor to produce oligodendrocytes, and  
(d) causing said oligodendrocytes to come into contact with a demyelinated axon to effect remyelination of said demyelinated axon.

19. A method for the *in vivo* proliferation of a precursor cell located in the CNS  
25 tissue of a mammal, said method comprising administering at least one proliferation-inducing growth factor to said CNS tissue to induce the proliferation of said cell.

20. A method for the *in vivo* genetic modification of a CNS precursor cell located in tissue lining a CNS ventricle of a mammal, said method comprising

administering genetic material to said CNS ventricle to infect said cells, said genetic material being capable of encoding at least one neurological agent.

21. The method of claim 20 further comprising administering at least one proliferation-inducing growth factor to said ventricle to induce the proliferation of  
5 said cell.

22. A method of treating a neurological disorder of a mammal comprising administering a composition comprising a proliferation-inducing growth factor to a ventricle of the central nervous system of said mammal, said ventricle being lined by tissue comprising at least one precursor cell, said growth factor inducing the *in*  
10 *vivo* proliferation and, optionally, differentiation of said precursor cell to form tissue comprising proliferated precursor cells.

23. The method of claim 22 further comprising the additional steps of: removing said tissue comprising proliferated precursor cells, dissociating said tissue to separate said proliferated precursor cells, culturing said proliferate  
15 precursor cells in a culture medium <sup>(*serum*)</sup> *in vitro* containing a proliferation-inducing growth factor to further proliferate and, optionally, differentiate said precursor cells, and implanting said proliferated and/or differentiated precursor cells into said ventricle of said mammal.

24. The method of claim 22 further comprising the additional steps of: removing  
20 said tissue comprising proliferated precursor cells, dissociating said tissue, culturing said dissociated tissue comprising proliferated precursor cells in a culture medium *in vitro* containing a proliferation-inducing growth factor to further proliferate said precursor cells, genetically modifying said proliferated precursor cells with genetic material capable of encoding at least one neurological agent, and  
25 implanting said genetically modified precursor cells into said ventricle of said mammal.

25. A method of treating a neurological disorder of a mammal comprising administering genetic material to a CNS ventricle of a mammal, said ventricle

being lined by tissue comprising at least one precursor cell, said precursor cell being genetically modified *in vivo* by said genetic material, said genetic material being capable of encoding at least one neurological agent.

26. A method of transplanting neural stem cell progeny to a host comprising:

- 5 (a) obtaining neural tissue from a mammal, said neural tissue containing at least one multipotent neural stem cell capable of producing progeny that are capable of differentiating into neurons, and glia;
- (b) dissociating said neural tissue to obtain a cell suspension
- 10 comprising said multipotent neural stem cell;
- (c) culturing said cell suspension in a culture medium containing at least one proliferation-inducing growth factor to proliferate said neural stem cell and produce neural stem cell progeny; and
- (d) transplanting said neural stem cell progeny to said host.

15 27. The method of claim 26 wherein prior to step (d), said neural stem cell progeny are genetically modified to express a biological agent selected from the group consisting of growth factors, growth factor receptors, neurotransmitters, neurotransmitter synthesizing genes, neuropeptides, and chromaffin granule amine transporter.

20 28. A method for determining the effect of at least one biological agent on neural precursor cells comprising:

- (a) dissociating mammalian neural tissue containing at least one multipotent stem cell,
- (b) proliferating said multipotent stem cell in a culture medium containing
- 25 at least one growth factor to obtain a culture of proliferated precursor cells,
- (c) contacting said proliferated precursor cells with said biological agent, and
- (d) determining the effects of said biological agent on said precursor cells.

29. A method for determining the effect of at least one biological agent on the

differentiation of neural cells comprising:

- (a) dissociating mammalian neural tissue containing at least one multipotent stem cell,
- (b) proliferating said multipotent stem cell in a first culture medium
- 5 containing at least one growth factor to obtain a culture of proliferated precursor cells,
- (c) inducing said proliferated precursor cells to differentiate in a second culture medium in the presence said biological agent, and
- (d) determining the effects of said biological agent on the differentiation of
- 10 said precursor cells.

30. A method for determining the effect of at least one biological agent on differentiated neural cells comprising:

- (a) dissociating mammalian neural tissue containing at least one multipotent stem cell,
- 15 (b) proliferating said multipotent stem cell in a first culture medium containing at least one growth factor to obtain a culture of proliferated precursor cells,
- (c) inducing said proliferated precursor cells to differentiate into differentiated neural cells,
- 20 (d) contacting said differentiated neural cells with said biological agent, and
- (d) determining the effects of said biological agent on said differentiated neural cells.

31. A cDNA library prepared from neural stem cell progeny.